rates. The purpose of using different flow rates is to allow the clinician to "draw conclusions on the intensity and location of the inflammation in the lungs" see page 3, last sentence of paragraph **[0027]**. The clinician does this by using the data to differentiate between bronchial NO flux and alveolar NO concentration since the different flow rates, according to the document, reflect different tissues in the lungs. This is explained in paragraphs **[0030]** and **[0031]** of page 3. The examiner notes that Moilanen et al. mention an eight-week test, but while Moilanen et al. might have been able to derive a baseline from the measurements taken over this period, they do not report having done so, and no adjustments were made to the treatment protocol after comparing the results with a baseline or with deviations from a baseline.

> The examiner has also pointed to the following statement from paragraph **[0031]**:
>
> "The results also suggest that the present method can be used to follow-up drug treatment of inflammatory lung diseases and provide means to assess the efficacy of such treatment."

The "present method" in this statement refers to the measurement at different exhalation rates to get location-specific data, as explained in the preceding paragraphs. There is no suggestion in this statement of the frequency of the measurement needed to establish the baseline, or of the frequency or number of measurements over any period of time to determine the amount or direction of the change in measured NO levels, much less any tailoring of modifications of the treatment based on the degree and the direction of the change. The criticality of the time periods in establishing the baseline and in evaluating the drifts is not mentioned or suggested. All of these features are recited in Applicants' claims. Thus, the protocol and hence the process as a whole as presently claimed by Applicants is not disclosed or suggested by Moilanen et al.

The disclosure missing from Moilanen et al. is not supplied by Kharitonov et al. Kharitonov et al. disclose the use of exhaled NO for "monitoring" (p. 533, left col.) and "assessing the anti-inflammatory effect of inhaled asthma treatments" (p. 535, right col.), and state that "absolute values are less important than serial measurement in individual patients" (p. 536, left col.). There is no discussion of a comparison of detected values with a baseline, of the particular results that should initiate a modification, and of how the modification should be monitored. Nor is there sufficient disclosure to enable the person skilled in the art to take

measurements and process them in the manner presently claimed. The present claims recite parameters that are specifically directed to achieving control in any individual regardless of the environment or of any aberration or special circumstance in the individual's recent physiological history that might affect the measurement. By simply referring to "monitoring" and "serial measurement," Kharitonov et al. do not lead one to such features as a minimum frequency of measurement and a minimum length of time to allow a treatment modification to affect the subject's condition before considering further modification to the treatment protocol. By their own admission, Kharitonov et al. rely on "precise" measurement (p. 536, left col.), which is a reference to individual measurements rather than to trends.

To summarize, neither Moilanen et al. nor Kharitonov et al. disclose or suggest the frequency of the measurement needed to establish the baseline, or the frequency or number of measurements over any period of time to determine the amount or direction of the change in measured NO levels, much less any tailoring of modifications of the treatment based on the degree and the direction of the change, all as recited in Applicants' claims. This combination of references therefore fails to render claims 18-27 obvious.

Rejection of claims 18-24 over Hampton et al. (US 2003/0073919) in view of Moilanen et al. (US 2002/0193698)

This rejection is likewise traversed. The examiner's attention is directed to the fact that Applicants' claims are specifically directed to nitric oxide while the disclosure of Hampton et al. is strictly limited to carbon dioxide. The respiratory conditions giving rise to abnormalities in the amounts of these components in exhaled breath are not coextensive, and the treatment protocols and response to treatment differ as well. Applicants therefore submit that the disclosure of Hampton et al. is not relevant to the claims presently under examination.

Aside from the failure of Hampton et al. to even mention nitric oxide, the portions of the disclosure that the examiner has cited are paragraphs **[0013]** and **[0015]**, which read as follows (emphasis added):

> "**[0013]** The method *may* take into consideration, for example, the duration of a steady rise of the concentration of carbon dioxide in the breath or the rate of increase of the concentration of carbon dioxide, as measured by the initial angle and slope of the

> capnogram. The method *may* also compare the carbon dioxide concentration in the breath with a characteristic curve. The method *may* further include monitoring the condition of the patient following treatment.
>
> ...
>
> "**[0015]** In a further embodiment, the invention presents a method comprising measuring a concentration of carbon dioxide in a breath expired by a patient and guiding treatment as a function of the measurement. Guiding treatment *may* include determining the presence of lung conditions, determining the severity of the conditions, and selecting medications to treat the conditions."

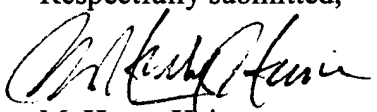
Due to their equivocal nature and their lack of specifics, the statements in these paragraphs do not amount to an "enabling description," i.e., they fail to supply the reader with sufficient explanation or detail to enable the reader to actually perform the tasks referred to in the paragraphs, and particularly of how to determine whether a rise is significant and how it compares to a baseline. The description in paragraph **[0013]** recognizes only a "steady rise" in analyte concentration rather than a rise defined by the rate of rise at a particular exhalation rate and the duration of the rise. Also, the "characteristic curve" of paragraph **[0013]** is neither explained, illustrated, nor demonstrated. It could mean anything at all and its meaning is left up to the reader to determine. The determinations that a person skilled in the art would have to make in order to perform the indicated tasks to any degree of effectiveness for any analyte, much less one that is not even mentioned in the document, would amount to an independent action of invention.

These shortcomings of the disclosure of Hampton et al. are not met by the disclosure of Moilanen et al. which has been discussed in detail above. Thus, neither of these two references disclose or suggest the frequency of the measurement needed to establish the baseline, or the frequency or number of measurements over any period of time to determine the amount or direction of the change in measured NO levels, much less any tailoring of modifications of the treatment based on the degree and the direction of the change, all as recited in Applicants' claims. The combination of Hampton et al. and Moilanen et al. thus fails to render claims 18-24 obvious.

CONCLUSION

In view of the foregoing, Applicants believe all claims pending in this Application recite patentable subject matter, and reconsideration of the application and the issuance of a Notice of Allowance are respectfully requested. Should any matters remain that can be resolved by a conference with Applicants' attorney, the examiner is encouraged to telephone the undersigned at 415-576-0200.

Respectfully submitted,



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